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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/913,631	01/16/2003	Charlotte Hauser- Funke	KGB	3848

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EXAMINER	
LIETO, LOUIS D	

ART UNIT	PAPER NUMBER
1632	

DATE MAILED: 12/02/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/913,631	HAUSER- FUNKE, CHARLOTTE	
	Examiner	Art Unit	
	Louis D. Lieto	1632	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *19 October 2005*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *50-115* is/are pending in the application.

4a) Of the above claim(s) *50-70,77-105 and 108-115* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *71-76, 106, and 107* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Applicant's response filed on 10/19/2005 is acknowledged. Claims 50-115 are pending. Claims 50-70, 77-105, and 108-115 have been withdrawn, and claim 71 was amended. Claims 71-76, 106, and 107 are under consideration. The sections of 35 U.S.C. not included in this office action can be found in a previous office action. An action on the merits follows.

Information Disclosure Statement

Applicant has submitted several foreign references and non-patent literature documents, which are on file. However, as applicant has noted I their reply an IDS has not been filed. In order to have the references printed on such resulting patent, a separate listing, preferably on a PTO/SB/08A and 08B form, must be filed within the set period for reply to this Office action.

Claim Rejections - 35 USC § 112

The rejection of claims 71-76, 106 and 107 under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement, is maintained. The claim(s) contains subject matter that was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to use the invention.

Response to Arguments

Applicant's arguments filed on 10/19/2005 have been fully considered but they are not persuasive. Applicant argues that Groups 1 and 5 in Figure 17 "appear" to show a statistical difference because the groups do not extensively overlap. A review of Figure 17 does not support

this argument. The error bars of Group 1 encompass the midpoint of group 5, indicating that there is no statistical difference between these two groups. The data shown in Figure 17 indicates that there is no statistically significant difference in coagulation time between groups 1 and 5.

Further, applicant argues that in Figure 18, overall Group 5 seems to show a longer coagulation time than group 1. However as previously stated: Figure 18 shows that on days 3 and 8 group 1 had the longest blood coagulation time of any of the test groups. This indicates that either successful gene transfer was not established, that the plasmid containing the nucleic acid construct was unable to express adequate levels of human factor IX over the time frame observed, or that expression of human factor IX in mice does not have a consistent effect on blood coagulation time. Further, careful review of Figure 18 shows that group 1 has a longer coagulation time than group 5 at days 5-8 and appears to have the same coagulation time during days 1-4. Between days 4-5 Group 5 appears to have a slightly greater coagulation time than group 1. Overall, the results do not suggest that plasmid has any consistent or long-term affect that differs from the control group.

Applicant argues that the references cited in the previous office action were outdated and do not represent the advances that were made at the time of filing of the claimed invention. Applicant is reminded that they must show enablement as of the earliest date to which they claim priority to, in this case 2/19/1999. The references cited in the prior office action were demonstrative of the state of the art during the time frame of filing of the provisional application. However, the following additional references are provided in order to demonstrate that the problems and inherent unpredictability with methods of gene therapy remain current problems in the art. Pfeifer and Verma state that even "though gene therapy holds great promise for the

achievement of this task, the transfer of genetic material into higher organisms still remains an enormous technical challenge {Pfeifer and Verma (2001) Annu. Rev. Genomics. Hum. Genet. 2:177-211; pg. 177, pgph 1}. Johnson-Saliba et al. concurs stating, "although thousands of patients have been involved in clinical trials for gene therapy, using hundreds of different protocols, true success has been limited. A major limitation of gene therapy approaches, especially when non-viral vectors are used, is the poor efficiency of DNA delivery." {Johnson-Saliba et al. (2001) Curr. Drug. Targets 2:371-99; Abstract}. Such problems with delivery continue to plague the field of gene therapy. Shoji et al. has characterized the current state of the art as the "tragic failure of gene therapy" because of poor delivery of gene based-medicines due to the lack of an appropriate vector that "fulfills the necessary requirements, including high transfection efficiency, non-toxicity, non-pathogenicity, non-immunogenicity, [and] non-tumorgenicity." {Shoji et al. (2004) Current Pharmaceutical Design 10 :785-796}. The rejection is maintained for the reasons stated above and in the previous office action of 4/20/2005.

Rejections under the second paragraph of 35 U.S.C. 112:

The rejection of claims 71-76, 106 and 107 under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention is maintained.

Response to Arguments

Applicant's arguments filed on 10/19/2005 have been fully considered but they are not persuasive.

Applicant has amended claim 71 to not incorporate their amendment. The new inserted language is crossed out, and the old original language is still present. Therefore the rejection is maintained overly the claim as presently drawn.

Applicant's argument in regards to the belief that the phrase "composition of matter is commonly used and accepted in patent claims, does not address the substantive issues raised in the prior action. The rejection is maintained for the reasons stated above and in the previous office action of 4/20/2005.

Claim Rejections - 35 USC § 102

Applicant has amended claim 71 to not incorporate their amendment. The new inserted language is crossed out, and the old original language is still present.

The rejection of claims 71, and 73-76 under 35 U.S.C. 102(b) as being anticipated by U.S Patent No 5,298,422 (1994), hereafter referred to as Schwartz[1] et al. is maintained.

Applicant has not amended the claims to "wherein one of said at least one HRE's does not regulate the transgene." Applicant's claims continue to broadly encompass any HRE. Claim 27 of Schwartz[1] et al. makes clear that the response element is the vitamin D response element, which is an HRE since vitamin D is classified as both a hormone and a vitamin. The rejection is maintained for the reasons stated above and in the previous office action of 4/20/2005.

The rejection of claims 71-76, 106 and 107 under 35 U.S.C. 102(b) as being anticipated by U.S Patent No US Patent No. 5,756,264 (1998), hereafter referred to as Schwartz[2] et al, is maintained

Schwartz[2] teaches a composition comprising the nucleic acid construct, Vitamin D and the Vitamin D receptor (Figure 13). Figure 13 shows that when the HRE binds vitamin D, this activates transportation, which appears to be the identical concept shown in Figure 1. The rejection is maintained for the reasons stated above and in the previous office action of 4/20/2005.

No claims allowed.

Conclusion

THIS ACTION IS MADE FINAL. Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to (571) 272-0547. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Dr. Lou Lieto whose telephone number is (571) 272-2932. The examiner can normally be reached on Monday-Friday, 9am-5 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Dr. Ram Shukla can be reached on (571) 272-0735. The fax phone number for the organization where this application or proceeding is assigned is (571)-273-8300. Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Patent applicants with problems or questions regarding electronic images that can be viewed in the PAIR can now contact the USPTO's Patent Electronic Business Center (Patent EBC) for assistance. Representatives are available to answer your questions daily from 6 am to midnight (EST). The toll free number is (866) 217-9197. When calling please have your application serial or patent number, the type of document you are having an image problem with, the number of pages and the specific nature of the problem. The Patent Electronic Business Center will notify applicants of the resolution of the problem within 5-7 business days. Applicants can also check PAIR to confirm that the problem has been corrected. The USPTO's Patent Electronic Business Center is a complete service center supporting all patent business on the Internet. The USPTO's PAIR system provides Internet-based access to patent application status and history information. It also enables applicants to view the scanned images of their own application file folder(s) as well as general patent information available to the public.

For all other customer support, please call the USPTO Call Center (UCC) at 800-786-9199.

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